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Spray Drying of Cubosomes for Oral Vaccine Delivery

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PURPOSE

To prepare cubosomes carrying the model antigen ovalbumin and the adjuvant Quil A using spray drying as method, as well as to *in vitro* characterize these particles.

METHOD

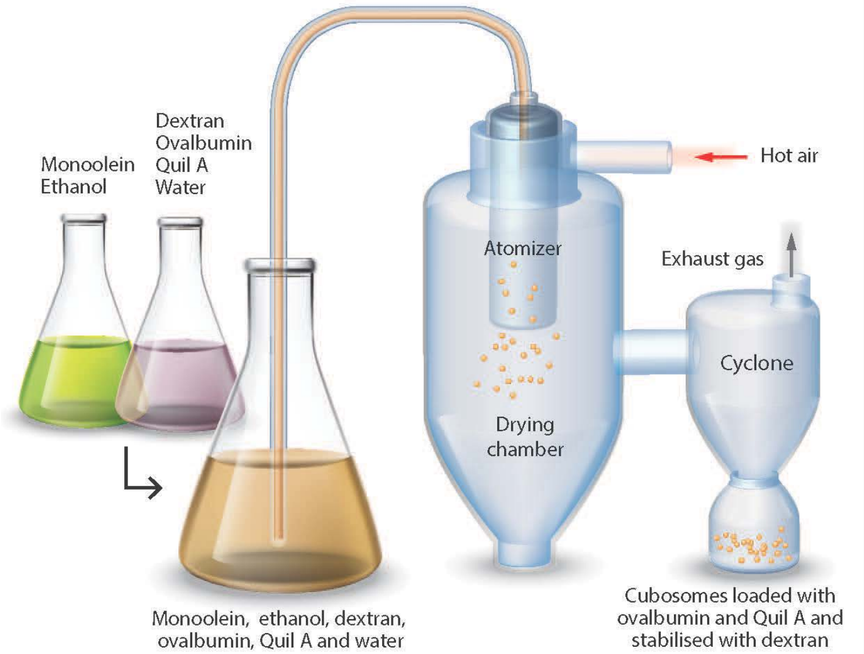

Fig. 1: 5.33 w/v% Dimodan® MO 90/D (high monoolein content) in ethanol is diluted by adding it to aqueous solution of dextran, ovalbumin (OVA) and Quil A (2.67, 0.13 and 0.14 w/v% respectively). The dilution of the ethanol causes immediate precipitation of lipid particles giving a turbid mixture in 24 v/v % ethanol. The mixture is spray dried on a Büchi mini spray dryer.

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RESULTS

Particle Morphology

The spray dried powder was heated to 90°C for 24h. This
- Reduced electrostatic charges in the powder
- Allowed easy reconstitution to a colloidally stable suspension
- Induced weight loss of 8%

The powder was rich in cubosomes after reconstitution (Fig. 2)

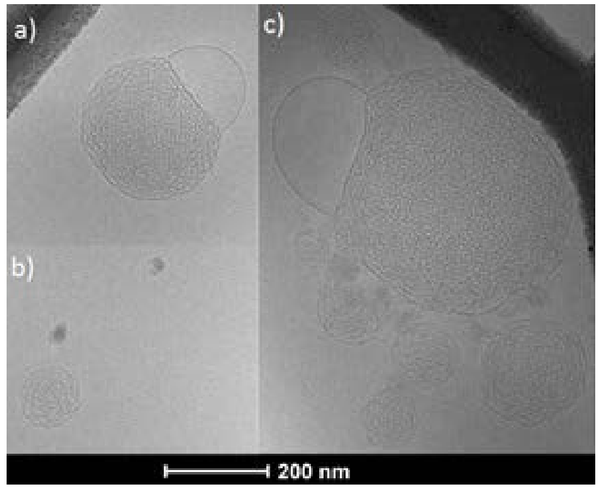

Fig. 2: Cubosomes produced from monoolein by a spray drying process. Representative cryo-TEM images of the cubosomes are shown immediately after reconstitution (a+b) and after 12 hours in suspension (c).

Ovalbumin release from cubosomes

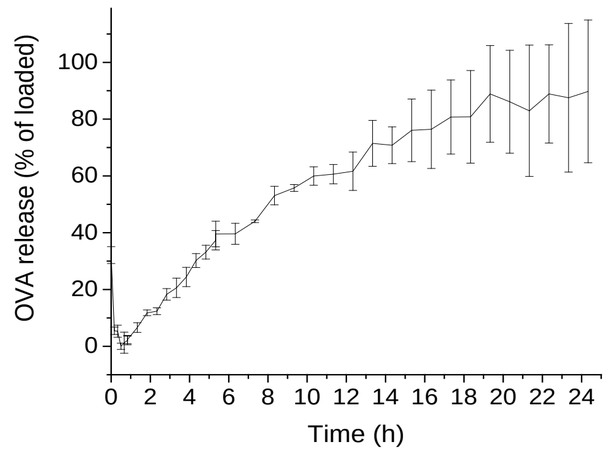

Fig. 3: Release kinetics of FITC-OVA from the cubosomes expressed as percent of total loaded FITC-OVA.

Particle Characterization

Table 1: Size and zeta-potential of cubosomes with and without adjuvant as measured by dynamic light scattering in Milli-Q water. Mass median aerodynamic diameter (MMAD) measured by time-of-flight mass spectroscopy.

Formulation	Size (nm)	PDI	Zeta potential (mV)	MMAD (µm)
Cubosomes with OVA	256±10	0.42	-31.7±1.4	4.1±0.4
Cubosomes with OVA and Quil A	233±13	0.24	-38.3±1.7	4.1±0.02

Table 2: OVA content in formulation

OVA content in powder	20.3±0.5 µg/mg
OVA load in particles	5.1±0.1% wt

Loading into microcontainers

Microcontainers were fully and homogenously filled with cubosome powder by an embossing method. The microcontainers offer the possibility to protect the formulation during passage through the stomach and provide release of the cubosomes in the intestine.

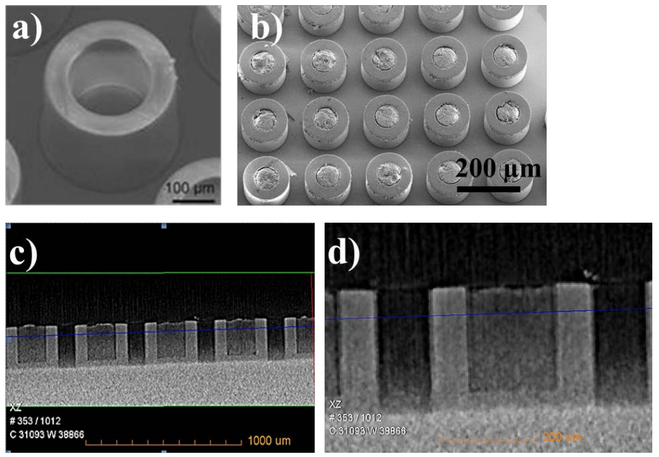

Fig. 4: a+b) SEM image of and empty microcontainer (a) and microcontainers loaded with cubosomes (b). c+d) X-ray microtomography images of the loaded microcontainers.

CONCLUSION

The developed cubosomes show properties suitable to be used for oral vaccine delivery in microcontainers.